

## AMENDMENTS

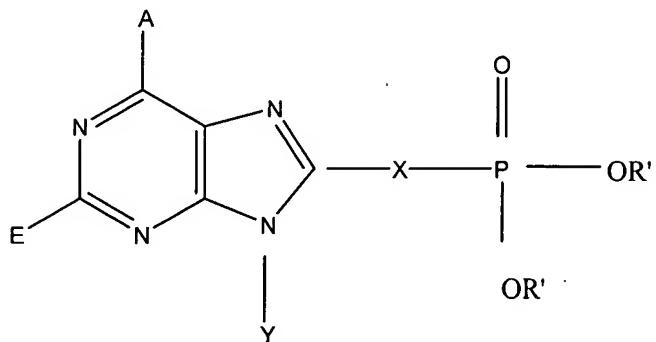
In the Specification:

Please amend the specification as follows:

at p. 122

ABSTRACT

Novel purine compounds of Formula 1, pharmaceutically acceptable prodrugs and salts thereof, the following structure and their use as fructose 1,6-bisphosphatase inhibitors is described.

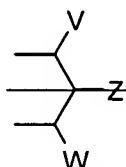
Formula 1

wherein

- A is selected from the group consisting of NR<sup>8</sup><sub>2</sub>, NHSO<sub>2</sub>R<sup>3</sup>, OR<sup>5</sup>, SR<sup>53</sup>)<sub>2</sub>, guanidino, amidino, H, and perhaloalkyl;
- E is selected from the group consisting of H, halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, CN, and NR<sup>7</sup><sub>2</sub>;
- X is selected from the group consisting of alk-NR<sub>6</sub>, alkylene, alkenylene, alkynylene, arylene, heteroarylene, alk-NR-alk, alk-O-alk, alk-S-alk, alk-S-, alicyclicene, heteroalicyclicene, 1,1-dihaloalkylene, C(O)-alk, NR-C(O)-NR', alk-NR-C(O)-, alk-C(O)-NR-, Ar-alk, and alk-Ar, all optionally substituted, wherein each R and R' is independently selected from H and lower alkyl, and wherein each "alk" and "Ar" is an independently selected alkylene or arylene, respectively;

— Y is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, alicyclic, heteroalicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl,  $C(O)R^3$ ,  $S(O)_2R^3$ ,  $C(O)OR^3$ ,  $CONHR^3$ ,  $NR^2$ , and  $OR^3$ , all except H are optionally substituted;

—  $R^1$  is independently selected from the group consisting of H, alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate,  $C(R^2)_2$  aryl, alk aryl,  $C(R^2)_2OC(O)NR^2$ ,  $NR^2C(O)R^3$ ,  $C(R^2)_2OC(O)R^3$ ,  $C(R^2)_2O-C(O)OR^3$ ,  $C(R^2)_2OC(O)SR^3$ , alk S  $C(O)R^3$ , alk S S alkylhydroxy, and alk S S S alkylhydroxy, or together  $R^1$  and  $R^1$  are alk S S alk to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together  $R^1$  and  $R^1$  are



— wherein

— V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1 alkenyl, 1 alkynyl, and  $R^9$ ; or

— together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy carboxy, or aryloxy carboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

— together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy carboxy, alkylthiocarboxy, hydroxymethyl, or aryloxy carboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

— Z is selected from the group consisting of  $CH_2OH$ ,  $CH_2OCOR^3$ ,  $CH_2OC(O)SR^3$ ,  $CH_2OCO_2R^3$ ,  $SR^3$ ,  $S(O)R^3$ ,  $CH_2N_3$ ,  $CH_2NR^2$ ,  $CH_2Ar$ ,  $CH(Ar)OH$ ,  $CH(CH=CR^2)OH$ ,  $CH(C=CR^2)OH$ , and  $R^2$ ;

— with the provisos that:

- a) ~~V, Z, W are not all H; and~~
- b) ~~when Z is  $R^2$ , then at least one of V and W is not H or  $R^9$ ;~~
- $R^2$  is selected from the group consisting of  $R^3$  and H;
- $R^3$  is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;
- $R^4$  is independently selected from the group consisting of H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;
- $R^5$  is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower alicyclic, and lower heteroalicyclic;
- $R^6$  is independently selected from the group consisting of H, and lower alkyl;
- $R^7$  is independently selected from the group consisting of H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and  $C(O)R^{10}$ ;
- $R^8$  is independently selected from the group consisting of H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic,  $C(O)R^{10}$ , or together said  $R^8$  groups form a bidendate alkylene;
- $R^9$  is selected from the group consisting of alkyl, aralkyl, alicyclic, and heteroalicyclic;
- $R^{10}$  is selected from the group consisting of H, lower alkyl,  $NH_2$ , lower aryl, and lower perhaloalkyl;
- $R^{11}$  is selected from the group consisting of alkyl, aryl, OH,  $NH_2$  and  $OR^3$ ; and pharmaceutically acceptable prodrugs and salts thereof.